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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,412	12/23/2005	Kwang-Kyun Park	69506(301067)	3068

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,412	PARK ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 are presented for examination

Priority

This application is a 371 of PCT/KR2004/001526, filed June 24, 2004, and claims foreign priority to Korean Application No. 10-2003-0040937, filed June 24, 2003.

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

No Information Disclosure Statement has been filed in the present application. Applicants are reminded of their duty to disclose information known to them to be material to the patentability of the present claims.

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR

1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The instant claims recite suppressants of toxicity induced by a cancer chemotherapeutic agent comprising xanthorrhizol as an active ingredient.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by **WO 00/67711** (Published November 16, 2000) (newly cited).

WO '711 teaches processes for preparing xanthorrhizol and novel uses of the same (Abstract). An object of the invention is to provide xanthorrhizol as an active ingredient of

antibacterial agents (page 3, lines 12-14), including formulation into tablets, capsules, solutions, ointments, aerosols, pills, and injections in combination with pharmaceutically acceptable carriers (page 7, line 27 to page 8, line 15). Xanthorrhizol was dissolved in DMSO at concentrations of 0.001%, 0.0015%, and 0.002% and was demonstrated to have antibacterial activity of a concentration of 0.002% (Example 3-1).

The reference thus teaches a composition of matter comprising xanthorrhizol as an active ingredient.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by **Campos *et al.*** (Life Sciences, 2000, vol. 67, pages 327-333) (newly cited).

Campos *et al*. teach that compositions comprising xanthorrhizol as an active ingredient induce endothelium-independent relaxation of rat thoracic aorta (Abstract). Xanthorrhizol in concentrations of 1, 3, 10, 30, and 100 μg/mL (in DMSO) significantly inhibited precontractions induced by KCl, noradrenaline, or $CaCl_2$ (*id.*).

The reference thus teaches a composition of matter comprising xanthorrhizol as an active ingredient.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by **Itokawa *et al.*** (Chem. Pharm. Bull., 1990, vol. 33, no. 8, pages 3488-3492) (newly cited).

Itokawa *et al*. teach administration of 50 mg/kg of xanthorrhizol in a 0.5% solution of carboxymethyl cellulose in isotonic sodium chloride to mice bearing Sarcoma 180 ascites tumors

(Table II; page 3490; page 3492). The composition comprising xanthorrhizol was active in reducing tumor growth of the Sarcoma 180 ascites tumors.

The reference thus teaches a composition of matter comprising xanthorrhizol as an active ingredient.

Claims 1-3 rejected under 35 U.S.C. 102(e) as being anticipated by **Park *et al.*** (US 2005/0261162 A1; Published Nov. 24, 2005; Filed Mar. 22, 2002) (newly cited).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Park *et al.* teach pharmaceutical compositions for treating or preventing cancer comprising xanthorrhizol as an active principle (Abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Itokawa *et al.*** (Chem. Pharm. Bull., 1990, vol. 33, no. 8, pages 3488-3492) and **Kimura *et al.*** (J. Pharm. Pharmacol., 2000, vol. 52, pages 883-890) (newly cited) in view of **Park *et al.*** (US 2005/0261162 A1; Published Nov. 24, 2005; Filed Mar. 22, 2002).

Itokawa *et al.* teach as applied to claims 1-3, *supra*. Such teachings are applied herein in the same manner and in their entirety. The instant claims differ from Itokawa *et al.* in that they do not teach compositions comprising xanthorrhizol and a cancer chemotherapeutic agent (claim 4).

However, Kimura *et al.* teach that the cancer chemotherapeutic agent cisplatin (as recited in claim 5) has antitumor activity against Sarcoma 180 tumors implanted in mice (Abstract; Figure 1). A composition comprising cisplatin dissolved in 0.9% NaCl was used to treat the tumor-bearing mice (page 884, "Materials"). Kimura *et al.* thus teach a composition comprising a cancer chemotherapeutic agent (*i.e.*, cisplatin) that is effective in inhibiting the growth of the same tumor type (*i.e.*, Sarcoma 180) that xanthorrhizol inhibits the growth of as taught in Itokawa *et al.*

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to formulate an anti-cancer composition comprising cisplatin and xanthorrhizol for the purpose of inhibiting the growth of Sarcoma 180 tumors in mice. The skilled artisan would have been imbued with at least a reasonable expectation that such a composition would be effective in inhibiting the growth of Sarcoma 180 tumors in mice because each individual agent was known in the art to be useful for such a purpose. One would have been motivated to do so because each of the therapeutics has been individually taught in the prior art to be successful at inhibiting the growth of Sarcoma 180 tumors in mice when administered in a pharmaceutically acceptable composition. Moreover, the instant situation is amenable to the type of analysis set forth in *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant claims, one of ordinary skill in the art would have been imbued with at least a reasonable expectation of success that by combining xanthorrhizol with cisplatin as taught in Itokawa *et al.* in view of the teachings of Kimura *et al.*, one would achieve a pharmaceutical composition suitable for inhibiting the growth of Sarcoma 180 tumors in mice.

Secondly, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). In the instant case, it is well established in the art that combining two

known anti-cancer agents that are effective against the same type of cancer or tumor is very likely to result in a composition that is at least effective, if not more effective, than the individual anti-cancer agents administered alone. Further, as evidenced by Park *et al.*, xanthorrhizol induces apoptosis of cancer cells and suppresses the activity of COX-2 and iNOS which are related to tumor promotion and inflammatory reaction (Abstract; Fig. 7; Fig. 8; Fig. 11). Such inhibition of a main enzyme in the production of prostaglandins would predictably reduce the levels of these inflammatory mediators in patients having cancer.

With respect to the amount of xanthorrhizol as recited in claim 6 (*i.e.*, 0.01 to 10 times the weight of the cancer chemotherapeutic agent), it is well within the purview of the skilled artisan to modify the amounts of active agents in pharmaceutical compositions for the purpose of optimizing the therapeutic benefit of administration of such compositions. As such, it would have been obvious to one of ordinary skill in the art at the time of the invention to adjust the amounts of xanthorrhizol and/or cisplatin in the pharmaceutical composition suggested and motivated by the cited references with the reasonable expectation that a composition having more or less xanthorrhizol than cisplatin would also be effective in inhibiting the growth of Sarcoma 180 tumors in mice.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Mata *et al.* (J. Nat. Prod., 2001, vol. 64, pages 911-914) and Hwang *et al.* (Planta Med., 2000, vol. 66, pages 197-197) teach that xanthorrhizol has antibacterial properties, similar to the teachings of WO 00/067711. Ponce-Monter *et al.* (Phytotherapy Research, 1999, vol. 13,

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pages 202-205) teaches that xanthorrhizol inhibits the tonic contraction of rat uterus. All of the cited references teach compositions comprising xanthorrhizol as an active ingredient.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614